

# Random Chronic Stress Is a Major Cause of Pancreatic Cancer

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Pancreatic cancer is a major cause of US cancer death. It has risk factors that are preventable, such as cigarette smoking, excess weight, type 2 diabetes, excessive alcohol use and diabetes (**[Pernick, How Pancreatic Cancer Arises Based on Complexity Theory, 2021](#)**). It also has risk factors that are not, such as having blood groups A, B or AB (i.e. not O). This abstract discusses random chronic stress or bad luck, another major cause of pancreatic cancer that is not preventable (**[Curing Cancer Blog – Part 7 – Random Chronic Stress](#)**), which is also a major cause of lung cancer in nonsmokers (**[Pernick, How Lung Cancer Arises, Based on Complexity Theory, 2021](#)**).

This subject was discussed in the abstract below, which was not accepted at a recent conference. Although disappointing, the advantage of this rejection is that I can publish it without any restrictions. The full paper is at **<http://www.natpernick.com/PancreaticcancerFeb2021.html>**. I welcome your comments to **[Nat@PathologyOutlines.com](mailto:Nat@PathologyOutlines.com)**.

## Random Chronic Stress Is a Major Cause of Pancreatic Cancer

### Context

Pancreatic cancer is the third leading cause of US cancer death, projected to become #2 by 2030. Patients have a 5 year relative survival rate of only 10%. Unlike other cancers, there have been minimal improvements since the mid-1970s. Many cases have no apparent risk factors.

### Design

We analyzed the population attributable fraction (PAF) of known risk factors and estimated the proportion due to random chronic stress / bad luck. We then analyzed possible mechanisms for the initiation of pancreatic malignancy.

## **Results**

Random chronic stress accounts for 25-35% of US cases, calculated as 100% minus the PAF of known risk factors. It causes an estimated 2 cases per 100,000 people per year (age standardized), accounting for 13,360 age adjusted cases.

We define random chronic stress as seemingly random cellular “accidents” that cause network dysfunction, promoted by prolonged lifespans, that may propagate to surrounding networks and promote malignancy, including (a) DNA or related replication errors in noncancerous stem cells; (b) errors in how DNA is organized or modified by epigenetic events; (c) errors in the distribution of cell components during cell division; (d) failure to restore physical interactions between tissue components after cell division, such as contact inhibition and (e) immune system dysfunction that, for a particular patient, is ineffective at eliminating premalignant or malignant cells. The category of random chronic stress / bad luck may include cancer risk factors not yet discovered, too infrequent to achieve statistical significance or not clinically evident in a patient, such as chronic pancreatitis without symptoms or microscopic changes.,

Based on self-organized criticality, our cellular networks are poised at a critical state in which small disturbances rarely set off a cascade of changes in the initial network, with long periods in which minor changes accumulate with no apparent clinical or microscopic changes, followed by bursts of activity leading to obvious premalignant or malignant changes. In evolution, punctuated equilibrium acts similarly. This is in contrast to gradualism, or stepwise cancer progression, which is logical and predictable but does not accurately describe malignant progression or evolution.

In lung cancer, patients with no risk factors have superior survival compared to those with risk factors; for pancreatic cancer, this is true of nonsmokers vs. smokers, but data is otherwise limited.

## **Conclusion**

Due to these baseline rates of pancreatic and lung cancer, new cancers will continue to arise and a “world without cancer” is not foreseeable.